UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/539,212	06/17/2005	Olga N. Kovbasnjuk	60384(71699)	2349

49383 7590 10/22/2007

EDWARDS ANGELL PALMER & DODGE LLP
Client: JHU
P.O. BOX 55874
BOSTON, MA 02205

EXAMINER	
HUFF, SHEELA JITENDRA	
ART UNIT	**PAPER NUMBER**
1643	
MAIL DATE	**DELIVERY MODE**
10/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/539,212	KOVBASNJUK ET AL.	
	Examiner	Art Unit	
	Sheela J. Huff	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *13-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/19/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I, claims 1-12 in the reply filed on 8/30/07 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-12 are currently under consideration and claims 13-17 are withdrawn from consideration.

Priority

The instant set of claims has priority to 10/20/03 because the concept of treating all types of cancers is not supported by the provisional application.

Information Disclosure Statement

The IDS filed 9/19/05 has been considered and an initialed copy of the PTO-1449 in enclosed.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The hyperlink is found on page 26, at line 1.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. In claim 1, line the phrase "the B-subunit of Shiga toxin" has no antecedent basis.

b. In claim 3, the term "derived" renders the claim vague and indefinite because it is not clear how or if the cells are derivatized or if the cells are --obtained-- from the tissue.

c. In claim 12, the terminology "therapeutic moiety" renders the claim vague and indefinite. Is the therapeutic moiety for cancer treatment or treatment for a different disease?

Claims 1-9 and 11-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabled for a method of reducing of inhibiting invasiveness and metastasis of tumor cells expressing Gb3, does not reasonably provide enablement for the prevention of invasiveness and metastasis of tumor cells or

for a method of reducing of inhibiting or preventing invasiveness and metastasis of tumor cells not expressing Gb3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The specification clearly shows that the B-subunit of the Shiga Toxin can be used to inhibit or reduce invasiveness and metastasis of tumor cells expressing Gb3. The state of the art clearly discloses that the B subunit of the toxin binds to and is internalized into target cells expressing Gb3 (see page 1162, first column, last paragraph of Haicheur et al International Immunology vol. 15 p. 1161 (2003)). Therefore, in view of this one skilled in the art would not be able to use the B subunit of the toxin to inhibit or reduce metastasis or invasiveness of tumor cells not expressing Gb3.

Furthermore, with respect to the terminology "preventing" applicant has not shown that the B subunit of the toxin can prevent any disease. Prevention of cancer reads on cancer vaccines. The goal of tumor vaccination is the induction of tumor immunity to prevent tumor recurrence and to eliminate residual disease, however, Essell (J. NIH Res. 1995 7:46) reviews the current thinking in cancer vaccines and states that tumor immunologists are reluctant to place bets on which cancer vaccine approach will prove effective in the long run (see the entire document, particularly the last paragraph) and further states that no one is very optimistic that a single peptide will trigger an immune response strong enough to eradicate tumors or even to prevent the later growth of micrometastases among patients whose tumors have been surgically

removed or killed by radiation or chemotherapy (p. 48, para 6). In addition, Spitler (Cancer Biotherapy, 1995, 10:1-3) recognizes the lack of predictability of the nature of the art when she states that "Ask practicing oncologists what they think about cancer vaccines and you're likely to get the following response: "cancer vaccines don't work". As a venture capitalist of the director of product development at a large pharmaceutical company and you're likely to get the same response." (p. 1 para 1).

Furthermore, Boon (Adv. Can. Res. 1992 58:177-210) teaches that for active immunization in human patients we have to stimulate immune defenses of organisms that have often carried a large tumor burden. Establishment of immune tolerance may therefore have occurred and it may prevent immunization and several lines of evidence suggest that large tumor burdens can tolerate or at least depress the capability to respond against the tumor (p. 206, para 2).

Thus, in view of the contemporary knowledge in the art of the general lack of successful applications of vaccines for the prevention of human diseases as discussed above, as well as the unpredictability in the art pertaining to an immune response against in patients with large tumor burdens as discussed above, as well as the lack of sufficient guidance in the specification, one of skill in the art would be forced into undue experimentation in order to use the invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-5,7-10 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over LaCasse et al Blood vol. 88 p. 1561 (1995) in view of Marcato et al

Infection and Immunity vol. 70 p. 1279 (3/2002) and applicant's admission on page 6, lines 1-2 of the specification.

LaCasse et al disclose treatment of human B cell lymphoma from bone marrow in mice using Shiga toxin 1 (see entire reference). The reference also discloses that the toxin was administered after the cancer is present (see p. 1562, middle of first column). On page 6 of the specification, applicant admits the toxins are known to bind to Gb3 expressing cells, therefore it is expected that the cells of the reference are Gb3 expressing cells.

This reference does not disclose the use of the B subunit of Shiga toxin 1 or 2 and the limitations of claims 8-9 and 12.

Marcato et al discloses that it is the B subunit of the toxins (either Shiga toxin ! or 2) that are responsible for the toxicity.

In view of the disclosure of Marcato et al that the toxicity resides in the B subunit of either toxin, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to use the B subunit of either toxin in the treatment of the primary reference with the expected benefit of treating B cell lymphoma. Furthermore, "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). In view of this, it would have also been

obvious to use other known cancer treatment, such as radiation or chemotherapeutic agents in combination with the B subunit to treat B cell lymphoma.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheela J. Huff whose telephone number is 571-272-0834. The examiner can normally be reached on Tuesday and Thursday from 5:30am to 1:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sheela J. Huff

Sheela J Huff
Primary Examiner
Art Unit 1643

SJH